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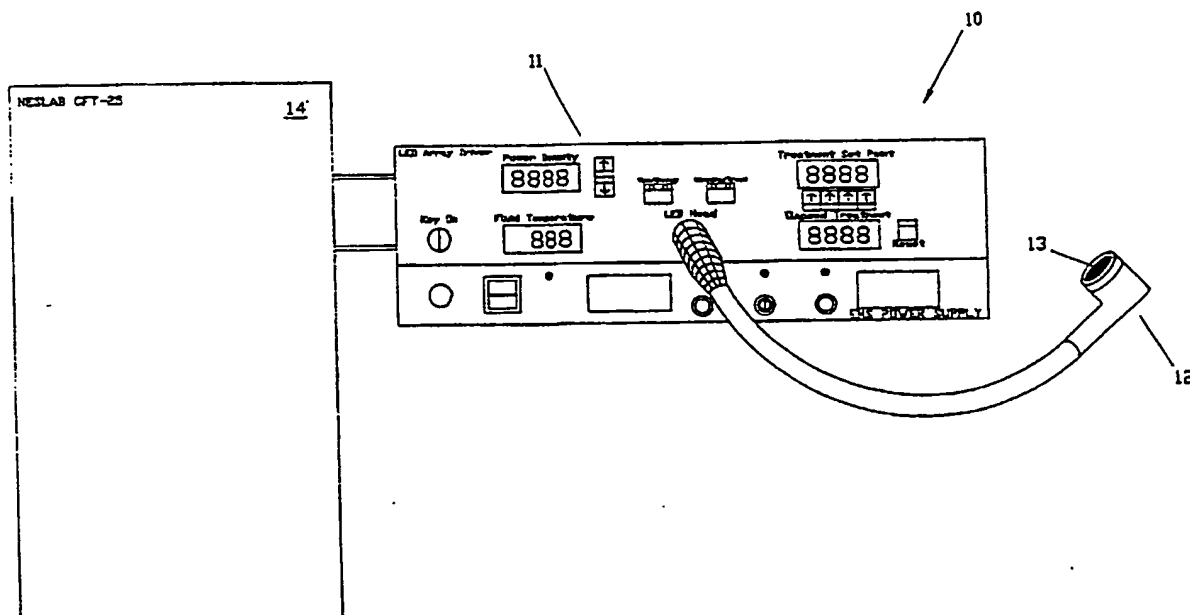
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International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁵ : A61N 1/00, 1/30, 5/00		A1	(11) International Publication Number: WO 94/15666
			(43) International Publication Date: 21 July 1994 (21.07.94)
(21) International Application Number: PCT/US94/00506		(81) Designated States: AU, CA, JP, RU, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).	
(22) International Filing Date: 12 January 1994 (12.01.94)			
(30) Priority Data: 08/003,537 13 January 1993 (13.01.93) US		Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	
(71) Applicant: PDT SYSTEMS, INC. [US/US]; 7408 Hollister Avenue, Goleta, CA 93117 (US).			
(72) Inventors: LYTLE, A., Charles; 1350 Primera Lane, Nipomo, CA 93444 (US). DALTON, Brian, K.; 3755 San Remo Drive, #255, Santa Barbara, CA 93105 (US). DUNN, Brian, J.; 551 Dawn Drive, Buelton, CA 93427 (US). DOIRON, Daniel, R.; 3090 Calzada Ridge Road, Santa Ynez, CA 93460 (US).			
(74) Agent: PEITT, Michael, G.; 510 Castillo Street, Santa Barbara, CA 93101 (US).			

(54) Title: LIGHT EMITTING DIODE SOURCE FOR PHOTODYNAMIC THERAPY



(57) Abstract

A system comprising a fluid cooled array of light emitting diodes (LEDs) for producing red (660 NM) light for photodynamic therapy is disclosed. The light is produced by a plurality of overdriven, water cooled LEDs arrayed on a preferably disposable puck. The LED puck (13) is releasably connected to an interchangeable LED hand piece (12). The system can be configured for illumination of flat surfaces such as for treatment of the chest or back, or for cylindrical surfaces such as found in the cervix or colon, by proper selection of the LED hand piece (12) and puck design (13).

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LIGHT EMITTING DIODE SOURCE FOR PHOTODYNAMIC THERAPY

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to photodynamic therapy and more specifically to a light source for photodynamic therapy.

2. Acknowledgement

This invention was made with Government support under Grant No. 1R43CA55446-1 awarded by the Department of Health and Human Services. The Government has certain rights in the invention.

3. Prior Art

Photodynamic therapy (PDT) is presently undergoing extensive basic pre-clinical and clinical testing and development both domestically and internationally. The general method of performing PDT is now well known and described, for example, in U.S. Patents 4,968,715; 4,932, 934; and 5,028,621 to Dougherty, et al.; and 5,002,962 to Pandey, et al. In PDT, photosensitizing drugs such as hematoporphyrin derivatives are introduced into and retained by the hyperproliferating cells or tissue such as cancerous tissue and atheromas. With the exposure to suitable wavelengths of light the photochemical reaction of the photosensitizer can lead to selective destruction of photosensitizer-associated cells or tissue. PDT also holds potential for a number of possible applications other than cancer treatment such as for treating microvascular lesions and blood purging. To obtain the desired therapeutic response, all of these applications require the delivery of sufficient light of appropriate wavelength to the photosensitizer in vivo. The

1 activating light must be sufficiently intense at wavelengths
2 matching the absorption spectrum of the photosensitizer to initiate
3 the photochemical reaction. Secondly, these wavelengths need to
4 penetrate the host tissue to permit activation of the therapeutic
5 reaction at the desired depth. Additionally, the light must be
6 able to be delivered to the treatment area in sufficient quantities
7 to permit treatment on a reasonable and effective time scale.

8 Prior art sources of illumination have been primarily
9 lasers. The reasons for this are the efficient deliverability of
10 the laser light through flexible single optical fibers, the single
11 wavelength nature of the laser, the tunability of certain lasers,
12 and the ability to deliver sufficient effective power to permit
13 reasonable treatment times. All of these properties together have
14 permitted PDT to be administered endoscopically with the
15 interstitial delivery of the light for the treatment of otherwise
16 inaccessible or large thick lesions. The use of lasers has not
17 been without drawbacks. These negative qualities of the laser
18 include high cost, low reliability, large size, complex operating
19 procedures and constant attention to the safety issues required
20 when dealing with laser light.

21 Puliafito, et al. (Arch. Ophthalmology, Vol 105, March,
22 1987) disclose using laser diodes for Photodynamic therapy. There
23 are significant differences between LED's and laser diodes. A
24 Light Emitting Diode (LED) is a solid state electronic device
25 capable of emitting light when an electric current is passed
26 through the device. LED-derived light is relatively broad band
27 (20-40nm) and is emitted in a wide output distribution pattern, and

1 lacks coherence. The light is produced at very low current levels
2 (20ma). All of these characteristics of LEDs serve to technically
3 differentiate them from laser diodes. The major advantage gained
4 by using a laser for PDT is the ability to couple significant light
5 power into flexible optical waveguides. This is necessary for
6 applications requiring interstitial or endoscopic delivery of
7 treatment light for PDT. Laser diode systems which include a large
8 power supply and cooling system are very expensive.

9 There are a significant number of applications for PDT
10 that do not require the use of a laser light source or the delivery
11 of light through light guides. In fact, the majority of the basic
12 pre-clinical and original trials of PDT using hematoporphyrin
13 derivative were done using non-laser light sources. For example
14 the treatment of cutaneous and subcutaneous skin lesions less than
15 1.0 cm thick can be treated using non-laser light sources. Skin
16 cancer incidence in the United States of America is over 550,000
17 new cases per year and rising. Even though a majority of these
18 cases can be easily treated with local resection or other methods,
19 there are a significant number involving multiple and/or recurrent
20 lesions that could be more conveniently treated using PDT. The
21 clinical use of PDT in many of these cases would be limited, in
22 part, due to the need to use lasers. This is due to the high cost
23 and lack of availability of suitable lasers. There is truly a need
24 for a low cost non-laser light source for use in PDT.

25 There are a number of non-laser light sources that could
26 potentially be used in certain PDT applications. The major
27 properties of these light sources that determine their

1 applicability in PDT are: a) output spectrum; b) brightness or
2 intensity at a suitable wavelength; c) deliverability; d) size;
3 and e) cost. These non-laser light sources include arc lamps,
4 incandescent lamps, fluorescent lamps and light emitting diodes
5 (LEDs). The lamp sources have a broad emission spectrum ranging
6 from ultraviolet to infrared. These broad spectrum sources require
7 the use of optical filtering to remove the undesired wavelengths,
8 particularly the ultraviolet and infrared, due to the potential of
9 carcinogenic effects and heating respectively. In addition, the
10 low brightness of these light sources at suitable wavelengths,
11 compared to lasers, make them all poor candidates for transmitting
12 sufficient power through small (less than 600 micron core),
13 flexible light guide to effect PDT. The best of these light
14 sources for brightness is the arc lamp due to the relatively high
15 intensity and small size of the discharge arc. Even though such
16 technology shows promise for certain medical applications,
17 including PDT, it still suffers from problems such as the need for
18 extensive filtering, limitations on its use for large area
19 exposure, and the requirement for high voltage and the concomitant
20 potential for arc lamp explosion.

21 LED technology, unlike the other non-laser light source
22 outlined above, has the advantage of small size, typically 0.3 mm
23 by 0.3 mm, limited emission spectrum band, typically 20 nm to 40
24 nm, high efficiency and low cost. The light power emitted from a
25 single diode is relatively low however (approximately 4 milliwatts
26 to 5 milliwatts for the brightest red LEDs using the specified
27 driving currents) but its emission angle is low when compared, for

1 example, to the arc lamp so that its actual brightness is
2 reasonably good. The small size of the LED along with its high
3 efficiency give the potential of using an array consisting of
4 multiple LEDs in a single device to significantly increase
5 deliverable power density over a large area. The low power output
6 has, however, delayed the acceptance of LED arrays as a suitable
7 light source for PDT. The intensity can be increased by over-
8 driving the LEDs in the array. Such over-driving results in
9 heating which shortens the lifetime of the LED and causes a
10 spectral shift in the output. LEDs are available in variety of
11 discrete packages as well as several one and two-dimensional array
12 packages. As used herein, an LED array means multiple LED's
13 integrally mounted in a single device. Commercially available
14 arrays, from manufacturers such as Mitsubishi, Hewlett Packard or
15 Stanley Electric, combine a few LEDs in a single package but not
16 in high enough packing density or in geometrics suitable for PDT.
17 None of these prior art devices can provide sufficient power
18 density for effective PDT treatments, nor can they be easily
19 configured in the geometries necessary for the wide range of
20 applications for surface illumination and PDT. It is desirable to
21 have a multiple integrated LED array with a power output suitable
22 for use in PDT.

23 SUMMARY OF THE INVENTION

24 It is an object of this invention to provide an array of
25 multiple integrated LEDs useful for photodynamic therapy.

26 It is another object of the invention to provide an
27 inexpensive light source useful for photodynamic therapy.

1 It is still another object of this invention to be able
2 to provide an LED array for photodynamic therapy that is capable
3 of illuminating the surface of various types of tissues.

4 It is yet a further object of this invention to provide
5 an LED array for photodynamic therapy which enables accurate
6 wavelength and exposure control and permits accurate dosimetry.

7 It is another object of this invention to provide an
8 illuminating system for photodynamic therapy that is safe to both
9 the physician and the patient.

10 The LED light source of the present invention is novel
11 because it teaches how to use the characteristics of the LED to an
12 advantage over the laser diode for applications of PDT which do not
13 require interstitial or endoscopic light delivery. The wide output
14 distribution pattern, small size, and minimal cooling requirements
15 of the LED allow large arrays of the devices to be constructed
16 which cumulatively are capable of producing a total output light
17 power exceeding that of laser diodes. This opens up applications
18 for large surface area illumination (such as is needed in
19 dermatology) for which laser diode systems are inadequate.

20 These and other objects of the invention will soon become
21 apparent as we turn now to a brief description of the drawings.

22 23 BRIEF DESCRIPTION OF THE DRAWINGS

24 Figure 1 is a schematic representation of an LED system
25 suitable for illumination of surfaces for photodynamic therapy.

1 Figure 2 schematic diagram of the front panel of the LED
2 array driver showing the displays for controls for exposure power
3 and coolant temperature display.

4 Figure 3 is a cross-sectional view of the LED handpiece
5 configured for flat surface illumination.

6 Figure 4 is a top view of the LED puck configured for
7 flat surface illumination.

8 Figure 5, which is a detailed top view of the area shown
9 in Figure 4 enlarged for ease of viewing, shows the top surface of
10 the LED puck showing the machine holes and indicating the LED die.

11 Figure 6 is a cross-sectional view of the LED handpiece
12 for illumination of cylindrical surfaces.

13 Figure 7 shows the LED sleeve for cylindrical surface
14 illumination.

15 Figure 8 is a schematic diagram of a preferred embodiment
16 of the light output and wavelength detector.

17 DESCRIPTION OF THE PREFERRED EMBODIMENT

18 It is the combination of small size and high efficiency
19 that make the LED a potentially useful light source for PDT. The
20 small size of the LED allows them to be fabricated in high density
21 into applicators of various shapes for the direct contact treatment
22 of cutaneous lesions. The shape may be circular, rectangular (or
23 any curvilinear surface) for treating skin lesions or cylindrical
24 for the treatment of cervical cancer. Planar arrays of LED's may
25 be bent or folded to form various curvilinear surfaces to conform
26 to the surface being treated. To be useful, the LED's must be
27 overdriven to produce useful power outputs. The heat generated

1 during over-driving must be removed by cooling the LED in order to
2 control the wavelength and increase the lifetime of the LED.

3 Turning now to Figure 1, we see a schematic view of the LED system
4 configured for flat surface illumination and generally indicated
5 at the numeral 10. The system consists of the LED array driver 11,
6 the flat surfaced LED handpiece 12, the flat surfaced LED puck 13
7 and the closed loop chiller 14. The detailed controls of the front
8 panel of the system are shown in Figure 2 of the array driver 11,
9 and shows the displays for the controls of exposure 21, power 22,
10 the coolant temperature display 23 and the power supply 24.

11 An LED handpiece configured for flat surface illumination
12 is shown in cross section in Figure 3. The stainless steel
13 housing 31 and threaded retaining ring 32 are connected to the
14 system ground 33 and provide one electrical connection to the LED
15 puck 13. The heat sink 34 is connected to the LED supply voltage
16 35. This provides the second electrical connections to the LED
17 puck as well as removing the heat generated in the puck. The heat
18 sink is electrically insulated from the housing by the DELRIN®
19 insulator 36. The coolant tubes 37 provide a flow of cooling water
20 from the chiller to the heat sink. The light output power and
21 wavelength detector 38 (shown in greater detail in Figure 8)
22 detects the amount of light being delivered to the patient by
23 sensing the light through the light sense channel 39.

24 An LED puck configured for flat surface illumination is
25 shown in Figure 4. The puck, generally indicated at 13, comprises
26 a gold plated insulated copper and fiberglass laminate sheet 41
27 bonded to a flat copper substrate 42. Holes are machined through

1 the copper laminate to the surface of the copper substrate. The
2 LED puck is coated with a clear epoxy potting material 43 to
3 protect the LED device and provide a smooth clean surface for
4 patient contact.

5 Figure 5, shown as detail A of Figure 4, is an enlarged
6 view of the top surface of the LED puck showing the machined holes
7 and indicating the LED die 51 bonded to the copper substrate 42
8 with electrically and thermally conductive epoxy 52. The figure
9 also shows the gold bonding wire 53 attached between the top
10 contact of the LED die and the surface of the copper laminate 41
11 using common integrated circuit assembly techniques.

12 Figure 6 shows a cross sectional view of the LED
13 handpiece for illumination of cylindrical surfaces, generally
14 indicated by 60. The stainless steel housing 31, threaded
15 retaining ring 32, coolant tubes 37, the photodiode detector 34 and
16 the insulator 36 function the same as in the flat surface
17 illuminating handpiece. The heat sink 61, the light sense channel
18 62 and the LED sleeve 63 are now shaped appropriately for insertion
19 into the cervical canal or rectum.

20 Figure 7 shows an LED sleeve configured for cylindrical
21 surface illumination 63. The copper laminate 71, copper substrate
22 72 and LED 73 are assembled in a similar manner to the flat surface
23 LED puck except the geometry is out of a tube instead of a disk.

24 The light output power and wavelength detector is shown
25 in greater detail in Figure 8. The light transmitted through the
26 light sense channel 39 (Figure 3) is focused by the collimating
27 lens 81 and split into two equal light beams by the beamsplitter

1 82. The light power in one beam path is filtered by a filter 83,
2 and measured by the photodiode 85. The unfiltered photodiode 84
3 measures the light power in the other light beam path. Assuming
4 that proper calibration is done to compensate for the different
5 optical losses in each path, the total optical power and
6 verification of the wavelength can be accomplished with this
7 technique. It is clear that this device could also be configured
8 with a flexible light guide (not shown) built into the handpiece
9 which would then deliver the sampled light energy to the light
10 power output and wavelength detector shown in Figure 8 which could
11 conveniently be installed in the LED array driver 11.

12 In summary, it has been shown that an LED array can be
13 configured to provide power and wavelength outputs suitable for
14 PDT. In order to achieve the required power levels, it is
15 necessary to over-drive the LED's. The additional current required
16 for over-driving generates heat at the diode junction which results
17 in: (a) a red-shift and broadening of the output light; and (b) a
18 shorter lifetime. To overcome these problems, the LED array is
19 mounted on a puck enabling the LED array to be cooled to control
20 the bandwidth and wavelength of the output light and increase the
21 lifetime of the array. In practice, the output wavelength depends
22 on the diode's junction temperature. Monitoring the wavelength
23 permits adjustment of the coolant temperature and flow rate to
24 maintain the junction at the desired temperature.

25 The foregoing preferred embodiment of the LED system for
26 photodynamic therapy provides a low cost, high power excitation
27 source for PDT which can be produced in a variety of shapes used

1 in a wide variety of applications. This device will allow PDT to
2 become viable treatment modality for many more cancer patients
3 inasmuch as it will now be cost effective for the physician's
4 office or small clinic. Although the invention has been described
5 in terms of particular embodiments and applications, one of
6 ordinary skill in the art in the light of this teaching, can
7 generate additional embodiments and modifications without departing
8 from the spirit of or exceeding the scope of the claimed invention.
9 For example, single LED chips may be fabricated into an array by
10 depositing them directly onto a chilled substrate by techniques
11 currently used in hybrid circuit fabrication. Accordingly, it is
12 to be understood that the drawings and descriptions herein are
13 preferred by way of example to facilitate comprehension of the
14 invention and should not be construed to limit the scope thereof.

CLAIMS

What we claim is:

1. An incoherent light source suitable for administering illumination for photodynamic therapy, said incoherent light source comprising, in combination: a) an LED array driver; b) an LED array; and c) a cooling means.

2. The light source of Claim 1 wherein the LED array is in thermal communication with said cooling means.

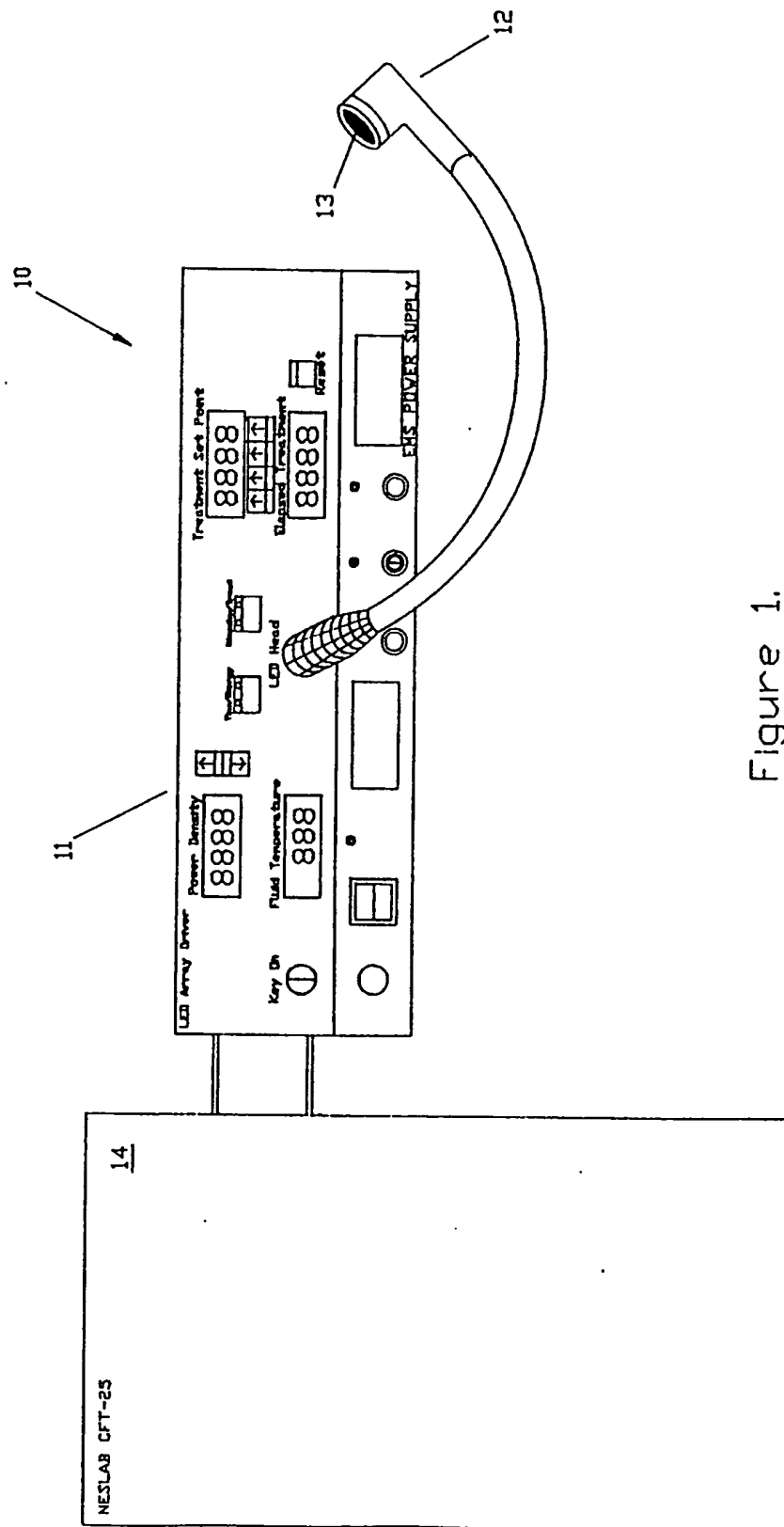


Figure 1.

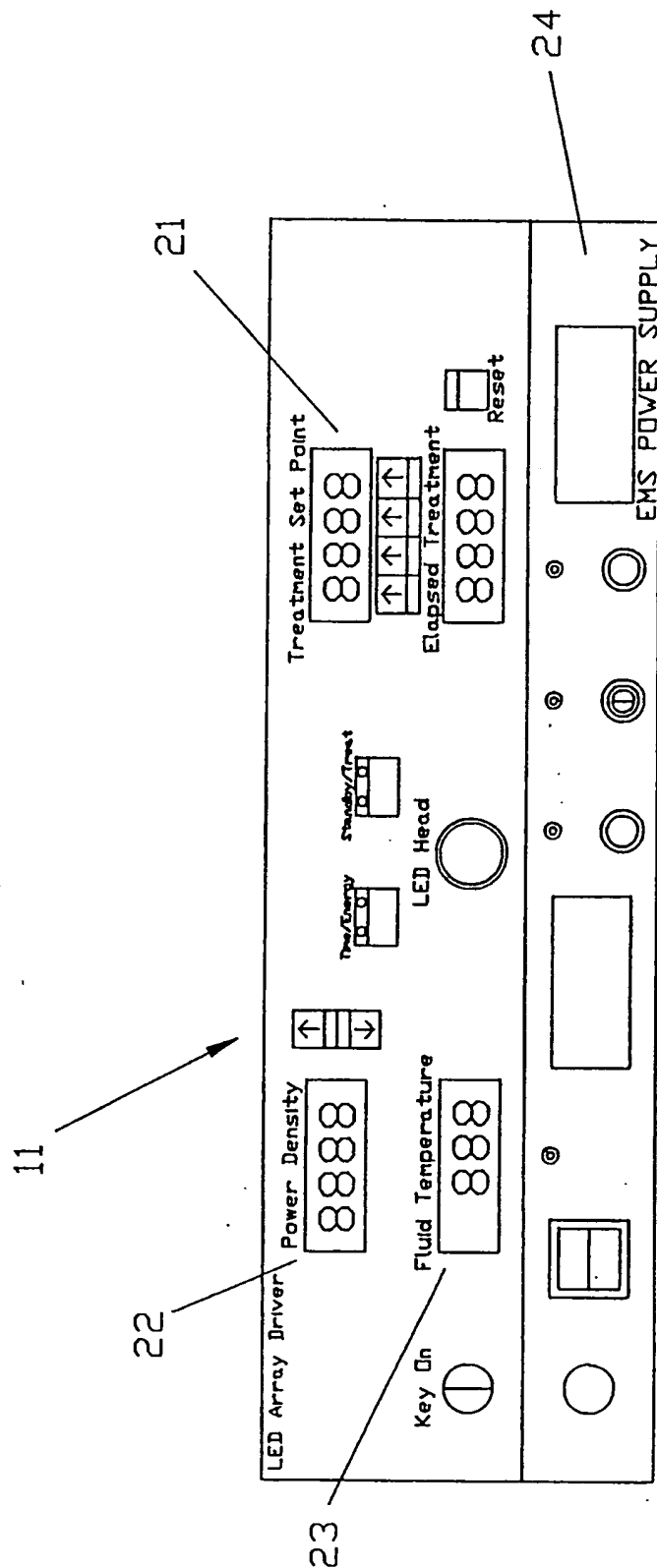


Figure 2.

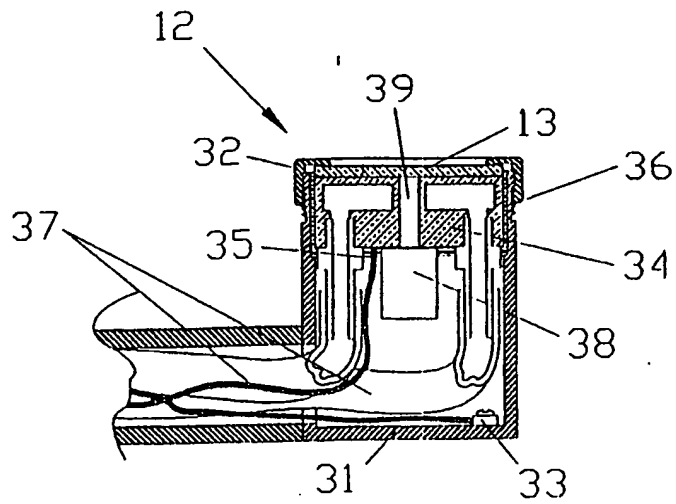


Figure 3.

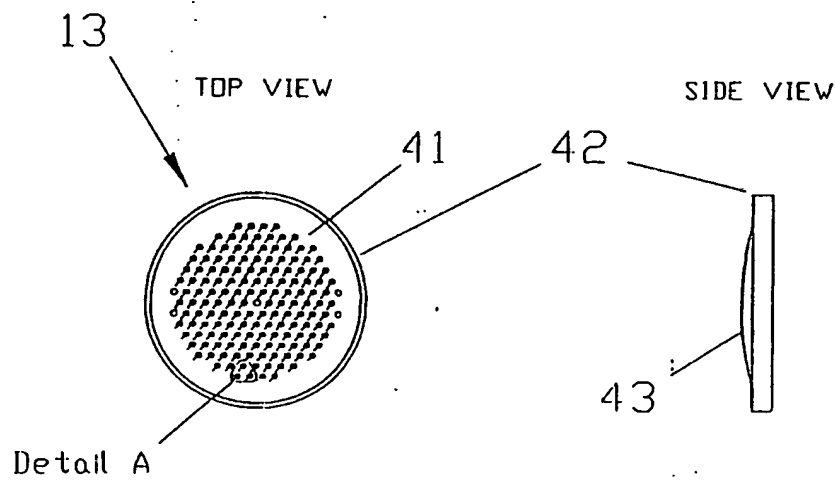


Figure 4.

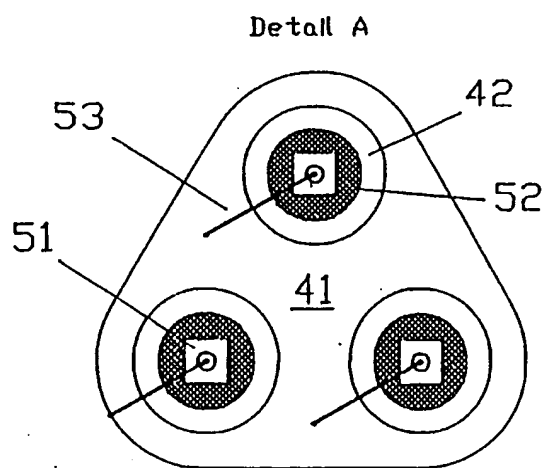


Figure 5.

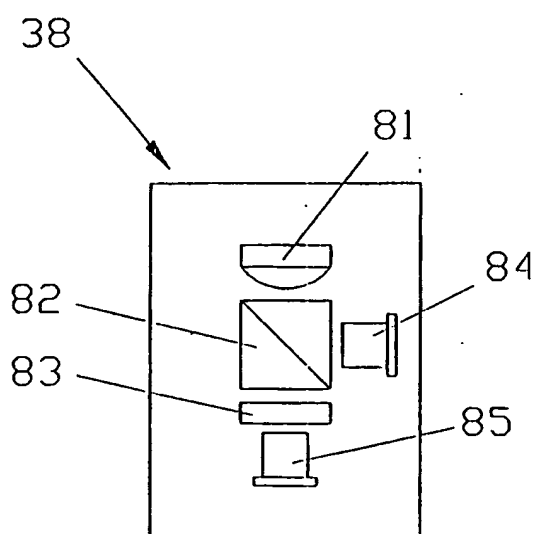


Figure 8.

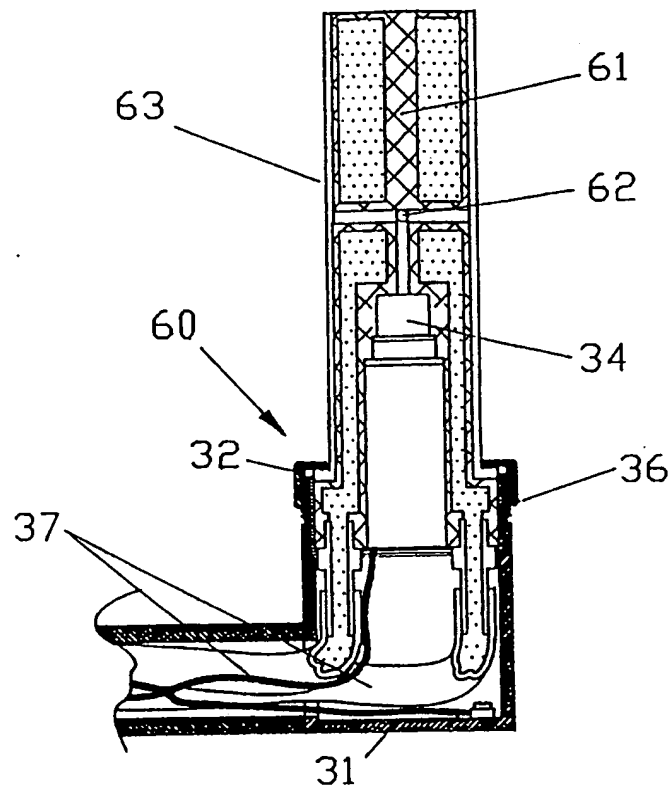


Figure 6.

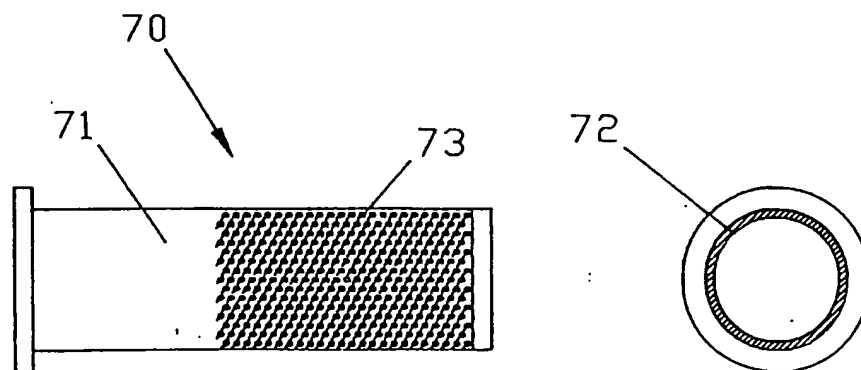


Figure 7.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/00506

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) : A61N 1/00, 1/30, 5/00

US CL : 128/395; 604/20; 606/4

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/395, 396; 514/410; 604/20; 606/4

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
None

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
None

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Journal of ARCH OPHTHAIMOL --- Vol 105, March 1987, pp. 424-427, Semiconductor Laser Endophotocoagulation of the Retina, CARMEN A. PULIAFITO, MD ET AL.	1-2
Y	US, A, 5,171,749, (LEVY ET AL.), 15 December 1992. See entire document.	2
A	GB, A, 2 212 010, (LISON ET AL.), 12 July 1989. See entire document.	

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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Date of the actual completion of the international search

03 MARCH 1994

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Name and mailing address of the ISA/US
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Facsimile No. (703) 305-3230

Authorized officer

JEROME KRUTER

Telephone No. (703) 308-2114